

REMARKS

Claims 1-114 are pending in this application. No claims have been allowed. The specification in paragraph [0060] has been amended to recite the limitations of claims 67. Support is provided in claim 67 as originally filed. Applicants note that information contained in any one of the specification, claims or drawings of the application as filed may be added to any other part of the application without introducing new matter. MPEP 2163.06. Accordingly, no new matter is entered by this amendment.

I. Objections to the Specification

The specification has been objected to for allegedly failing to provide proper antecedent basis for claim 67. Applicants have amended the specification at paragraph [0060] to include the terms of claim 67, “the highly crosslinked polymer comprises units derived from a radical reaction catalyzed by UV activation of bis(2,6-D, methoxybenzoyl)-2,4,4-trimethylphenyl phosphine oxide”. MPEP 2163.06.

II. Rejections under 35 U.S.C. § 103

1) Mathies in view of Alajoki

Claims 1-11, 55-64, 66, 68-77 and 111-114 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over U.S. Pat. App. No. 2004/0209354 to Mathies *et al.*, (“the Mathies application”) in view of U.S. Pat. App. No. 2002/0179445 to Alajoki *et al.* (“the Alajoki application”). Applicants respectfully submit that this rejection is improper because the office action does not set forth the basic requirements of a *prima facie* case of obviousness that is required by MPEP § 2143. To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. **The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure.** MPEP § 2143, *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438. Applicants submit that the office action does not properly set forth all three

of these requirements and therefore the rejection should be withdrawn. As set forth below, Applicants show how one of ordinary skill in the art would not be motivated to combine the Mathies and Alajoki applications to arrive at their claimed invention. Moreover, neither would one of ordinary skill in the art have a reasonable expectation of success in achieving Applicants' claimed invention in attempting to combine these applications.

The mere fact that references can be combined or modified does not render the resultant combination obvious **unless the prior art also suggests the desirability of the combination.** *In re Mills*, 916 F.2d 680, 16 USPQ2d 1430 (Fed. Cir. 1990). Claim 1 of the present invention, to which all of the claims depend on, recites a microfluidic chip comprising a plurality of vias; a functionalized porous polymer monolith capable of being in fluid communication with at least one of said vias; a microarray capable of being in fluid communication with said functionalized porous polymer monolith; and an observation port through which at least one target disposed within said microarray is capable of being detected. Applicants submit that neither the Mathies nor the Alajoki applications suggest the desirability of combining any of its disclosed microfluidic elements to arrive at Applicants' microfluidic chip **having an observation port through which at least one target disposed within said microarray is capable of being detected.** For example, the Mathies application describes microfluidic devices that have fluid control structures comprising monolithic elastomer membranes associated with an integrated pneumatic manifold for the placement and actuation of a variety of fluid control structures (abstract). **FIG. 11** in the Mathies application illustrates an embodiment of a microfluidic chip comprising *inter alia* an “Immuno-affinity Capture Chamber” 1101, which is fluidically connected to a separate PCR Chamber 1103, which is fluidically connected to a **separate** Capillary Electrophoresis (“CE”) channel 1113. Accordingly, one of ordinary skill in the art understands Mathies to teach that nucleic acids are first captured and purified in the Immuno-affinity Capture Chamber, and afterwards these nucleic acids are then fluidically transported to the PCR chamber for amplification. The resulting amplicons are subsequently fluidically transported to the CE microchannel for separation and detection. Accordingly, the locus of detection in the CE microchannel is spatially distinct from the locus of capture and purification in the Immuno-affinity Capture Chamber. The Office Action is therefore incorrect in alleging that such capture chambers, as described in paragraph [0079], can be used for the same purposes as

Applicants' microarrays. Whereas targets are disposed in Applicants' microarray and detected through an observation port, Mathies' capture chambers are described as being used to purify target molecules:

[0079] In other examples, each capture chamber is filled with a viscous polymeric matrix containing oligonucleotide probes to selectively bind the target molecules. In the case of DNA analysis, Sanger DNA sequencing extension products, including primers and polymerase reagents in a high salt concentration, are electrophoresed through an immunocapture chamber containing the immobilized acrylamide matrix containing the covalent oligonucleotide probe. The capture sequence is chosen so that only DNA amplification products are captured by the probe, but the primers and polymerase reagents, along with salts, pass through the device. **This is not unlike the need to purify target molecules from complex, dirty mixtures that will be encountered in point of care analyses.**

Mathies application, par. **[0079]**.

Nowhere does the Mathies application in paragraph **[0079]** teach or suggest that such bound, purified, target molecules are to be detected in its capture chambers in the way as Applicants' microarrays (i.e., capable of capturing at least one target which is capable of being detected through Applicants' observation port). In contrast, the Mathies device uses a much different method of detection, a **capillary electrophoresis ("CE") channel**, which is separate from the capture chambers:

[0071] According to various embodiments, **the immunoaffinity capture chambers 703, 713, and 723 are integrated with PCR chambers but CE mechanisms remain separate.** The combination of immunocapture and nucleic acid analysis dramatically enhances the sensitivity and specificity of the individual assays.

[0072] ... In many examples, **the processed samples can then be provided for CE analysis.**

[0073] Integrated immunoaffinity capture chambers are included in a pathogen analyzer. A variety of capture mechanisms can be used, such as frits, beads, gels, monoliths, and polymers. **FIGS. 8 and 9 are diagrammatic representations showing immunocapture chambers**

implemented using silica frits or beads. According to various embodiments, immunocapture chambers includes a series of silica flits fabricated by filling wafer holes with a mixture of silica power and sodium silicate binder. Upon dehydration and rinsing, the silicate condenses to silica gel and **an insoluble silica flit is formed at 801, 803, 805, and 807.**

(Mathies application, at the indicated paragraphs, emphasis supplied).

Thus, one of ordinary skill in the art would not be motivated to place an observation port over the capture chambers in the Mathies application because Mathies detects its analytes using separate capillary electrophoresis. Accordingly, the Mathies application does not teach one of ordinary skill in the art the desirability of looking elsewhere in the related art (such as the Alajoki application) to combine an observation port to its capture chambers. For these reasons, Applicants request that this rejection for alleged obviousness be withdrawn. Any claim depending from an independent claim nonobvious under 35 U.S.C. 103 is nonobvious too. *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Accordingly, all of the remaining claims 2-114, which depend from independent claim 1, are also nonobvious for these reasons.

Even if the Office has set forth a *prima facie* case of obviousness (and Applicants are not contending that it has), Applicants traverse the rejection under 35 U.S.C. §103(a) because the deficiency of the Mathies application (*e.g.*, providing a plurality of vias and an observation port through which at least one target disposed within the microarray is capable of being detected) is not cured by the Alajoki application. The Alajoki application discloses “Method and Apparatus for **Continuous Liquid Flow** in Microscale Channels using Pressure Injection, Wicking, and Electrokinetic Injection” (Title). Indeed, the Alajoki application provides “apparatus and methods for **modulating flow rates** in microfluidic devices” (Abstract). Accordingly, one of ordinary skill in the art would realize that the Alajoki application is concerned with **microfluidic devices that have continuous fluid movement through microchannels**. Likewise, molecules are continuously flowing within the microchannels while being detected through a detection window using Alajoki’s continuous flow device. See, for example, Alajoki paragraph [0089] which provides a partial description of **Figure 1**:

[0089] The microfluidic device includes a detection window or zone at which a signal is monitored. For example, reactants or assay components are contacted in a microfluidic channel in first region 115, and subsequently flowed into reading area 120, comprising a detection window or region. . . .

Alajoki application at [0089].

This is very different from Applicants' microfluidic chips which include a microarray and an observation port through which at least one target disposed within the microarray is capable of being detected. Importantly, Applicants' microarrays are generally "a collection of probes synthesized, attached or deposited on a substrate" (Specification, paragraph [0035]). Accordingly, if one of ordinary skill in the art were to combine the Mathies and Alajoki applications (and Applicants are not contending that there is motivation to do so), they would probably arrive at some kind of device that monitors the signals of an analyte continuously flowing through a microchannel, which is completely different than Applicants' microfluidic chip that is capable of detected targets disposed on a substrate. For these additional reasons, Applicants request that this rejection for alleged obviousness be withdrawn.

2) Mathies in view of Alajoki, and Schembri

Claims 16-25, 31-44, and 51-54 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over the Mathies application in view of the Alajoki application as applied to claims 2 and 11, and further in view of U.S. Pat. No. 6,875,620 ("the Schembri patent"). The Office Action asserts that the combination of Mathies and Alajoki discloses all of the required elements of Applicants' claimed invention as applied to claims 2 and 11 except for the inclusion of the use of probes that are disposed as at least one spot, or probes comprising an ordered arrangement. The Office Action then looks to the Schembri patent to supply a plurality of probes arranged on a plurality of tiles to form Applicants' claimed invention. Applicants respectfully traverse the rejection because there is no motivation to combine the references in the manner urged by the Examiner and because the combination of references does not disclose, teach or suggest the Applicants' claimed invention.

As Applicants described with respect to the nonobviousness discussion above, all of the claims dependent on claim 1, such as claims 2 and 11, are non-obvious with respect to the

combination of the Mathies and Alajoki applications. Accordingly, the additional combination of the Schembri patent's disclosure pertaining to a "plurality of spots" still does not overcome the deficiencies of the combination of the Mathies and Alajoki applications, namely to provide a microarray and an observation port through which at least one target disposed within the microarray is capable of being detected. Thus, the combination of the disclosures of Mathies, Alajoki and Schembri still would not produce any claimed invention.

Because the combination of references does not disclose, teach or suggest all of the required elements of the claimed invention, Applicants submit that Mathies in view of Alajoki, and further in view of Schembri does not render obvious the claimed invention and requests withdrawal of the rejection of claims 16-25, 31-44, and 51-54 under 35 U.S.C. § 103(a).

3) Mathies in view of Alajoki, and Yamamoto

Claims 12-15, 19, 25-35, 43-46 and 48-54 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over the Mathies application in view of the Alajoki application as applied to claims 2 and 11, and further in view of U.S. Pat. App. Pub. No. 2004/0209354 ("the Yamamoto application"). The Office Action asserts that the combination of Mathies and Alajoki discloses all of the required elements of Applicants' claimed invention as applied to claims 2 and 11 except for the inclusion of the use of thousands of probes that are arranged in an ordered or disordered plurality of spots. The Office Action then looks to the Yamamoto application to supply a plurality of probes arranged on a plurality of spots to form Applicants' claimed invention. Applicants respectfully traverse the rejection because there is no motivation to combine the references in the manner urged by the Examiner and because the combination of references does not disclose, teach or suggest the Applicants' claimed invention.

As Applicants described with respect to the nonobviousness discussion above, all of the claims dependent on claim 1, such as claims 2 and 11, are non-obvious with respect to the combination of the Mathies and Alajoki applications. Accordingly, the additional combination of the Yamamoto disclosure pertaining to a "plurality of spots" still does not overcome the deficiencies of the combination of the Mathies and Alajoki applications, namely to provide a microarray and an observation port through which at least one target

disposed within the microarray is capable of being detected. Thus, the combination of the disclosures of Mathies, Alajoki and Yamamoto would not produce any claimed invention.

Because the combination of references does not disclose, teach or suggest all of the required elements of the claimed invention, Applicants submit that Mathies in view of Alajoki, and further in view of Yamamoto does not render obvious the claimed invention and requests withdrawal of the rejection of claims 12-15, 19, 25-35, 43-46 and 48-54 under 35 U.S.C. § 103(a).

4) Mathies in view of Alajoki, and Klaerner

Claim 65 stands rejected under 35 U.S.C. § 103 as allegedly being unpatentable over the Mathies application in view of the Alajoki application as applied to claim 64, and further in view of U.S. Pat. App. Pub. No. 2002/0001845 (“the Klaerner application”). The Office Action asserts that the combination of Mathies and Alajoki discloses all of the required elements of Applicants’ claimed invention as applied to claim 64 except for the use of glycidyl methacrylate. The Office Action then looks to the Klaerner application to supply glycidyl methacrylate to form Applicants’ claimed invention. Applicants respectfully traverse the rejection because there is no motivation to combine the references in the manner urged by the Examiner and because the combination of references does not disclose, teach or suggest the Applicants’ claimed invention.

As Applicants described with respect to the nonobviousness discussion above, each claim that depends on claim 1, such as claim 64, is non-obvious with respect to the combination of the Mathies and Alajoki applications. Accordingly, the additional combination of the Klaerner disclosure pertaining to “glycidyl methacrylate” still does not overcome the deficiencies of the combination of the Mathies and Alajoki applications, namely to provide a microarray and an observation port through which at least one target disposed within the microarray is capable of being detected. Thus, the combination of the disclosures of Mathies, Alajoki and Klaerner still would not produce any claimed invention.

Because the combination of references does not disclose, teach or suggest all of the required elements of the claimed invention, Applicants submit that Mathies in view of Alajoki, and further in view of Klaerner does not render obvious the claimed invention and requests withdrawal of the rejection of claim 65 under 35 U.S.C. § 103(a).

5) Mathies in view of Alajoki, and Zare

Claim 67 stands rejected under 35 U.S.C. § 103 as allegedly being unpatentable over the Mathies application in view of the Alajoki application as applied to claim 62, and further in view of U.S. Pat. App. Pub. No. 2003/0062310 (“the Zare application”). The Office Action asserts that the combination of Mathies and Alajoki discloses all of the required elements of Applicants’ claimed invention as applied to claim 62 except for the use of “Irgacure 1800” during UV activation. The Office Action then looks to the Zare application to supply Irgacure 1800 to form Applicants’ claimed invention. Applicants respectfully traverse the rejection because there is no motivation to combine the references in the manner urged by the Examiner and because the combination of references does not disclose; teach or suggest the Applicants’ claimed invention. Moreoever, claim 67 does not recite the terms “Irgacure 1800”.

As Applicants described with respect to the nonobviousness discussion above, each claim that depends on claim 1, such as claim 62, is non-obvious with respect to the combination of the Mathies and Alajoki applications. Accordingly, the additional combination of the Zare disclosure pertaining to “Irgacure 1800” still does not overcome the deficiencies of the combination of the Mathies and Alajoki applications, namely to provide a microarray and an observation port through which at least one target disposed within the microarray is capable of being detected. Thus, the combination of the disclosures of Mathies, Alajoki and Zare still would not produce any claimed invention.

Because the combination of references does not disclose, teach or suggest all of the required elements of the claimed invention, Applicants submit that Mathies in view of Alajoki, and further in view of Zare does not render obvious the claimed invention and requests withdrawal of the rejection of claim 67 under 35 U.S.C. § 103(a).

6) Mathies in view of Alajoki, and Werner

Claims 78-90, 93, 94, 96, 97 and 106-110 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over the Mathies application in view of the Alajoki application as applied to claim 1, and further in view of U.S. Pat. App. Pub. No. 2002/0168652 (“the Werner patent”). The Office Action asserts that the combination of Mathies and Alajoki discloses all of the required elements of Applicants’ claimed invention as applied to claim 1

except for the inclusion of the use of a microarray capture zone disposed between a base substrate and a cover substrate. The Office Action then looks to the Werner application to supply such a microarray capture zone disposed between a base substrate and a cover to form Applicants' claimed invention. Applicants respectfully traverse the rejection because there is no motivation to combine the references in the manner urged by the Examiner and because the combination of references does not disclose, teach or suggest any claimed invention.

As Applicants described with respect to the nonobviousness discussion above, all of the claims dependent on claim 1, such as claims 78-90, 93, 94, 96, 97 and 106-110, are non-obvious with respect to the combination of the Mathies and Alajoki applications.

Accordingly, the additional combination of the Werner disclosure pertaining to, *inter alia*, microarray probes that are disposed on a top surface of a cover, or on the surface of a substrate, still does not overcome the deficiencies of the combination of the Mathies and Alajoki applications, namely to provide a microarray and an observation port through which at least one target disposed within the microarray is capable of being detected. Thus, the combination of the disclosures of Mathies, Alajoki and Werner still would not produce any claimed invention.

Because the combination of references does not disclose, teach or suggest all of the required elements of the claimed invention, Applicants submit that Mathies in view of Alajoki, and further in view of Werner does not render obvious the claimed invention and requests withdrawal of the rejection of claims 78-90, 93, 94, 96, 97 and 106-110 under 35 U.S.C. § 103(a).

7) Mathies in view of Alajoki, and Werner, and Christel

Claims 91 and 98-105 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over the Mathies application in view of the Alajoki and Werner applications as applied to claims 87 and 89, and further in view of U.S. Pat. No. 6,368,871 ("the Christel patent"). The Office Action asserts that the combination of Mathies, Alajoki and Werner discloses all of the required elements of Applicants' claimed invention as applied to claims 87 and 89 except for the inclusion of the use of specific microchannel dimensions or the use of microposts. The Office Action then looks to the Christel patent to supply specific microchannel dimensions and microposts to form Applicants' claimed invention. Applicants

respectfully traverse the rejection because there is no motivation to combine the references in the manner urged by the Examiner and because the combination of references does not disclose, teach or suggest the Applicants' claimed invention.

As Applicants described with respect to the nonobviousness discussion above, all of the claims dependent on claim 1, such as claims 87 and 89, are non-obvious with respect to the combination of the Mathies and Alajoki applications. Moreover, the additional combination of the Werner application does not render claims 87 and 89 obvious for the reasons given above. Accordingly, the additional combination of the Christel patent's disclosure pertaining to the specific microchannel dimensions and microsposts still does not overcome the deficiencies of the combination of the Mathies, Alajoki and Werner applications, namely to provide a microarray and an observation port through which at least one target disposed within the microarray is capable of being detected. Thus, the combination of the disclosures of Mathies, Alajoki, Werner and Christel still would not produce any claimed invention.

Because the combination of references does not disclose, teach or suggest all of the required elements of the claimed invention, Applicants submit that Mathies in view of Alajoki, further in view of Werner, and further in view of Christel does not render obvious the claimed invention and requests withdrawal of the rejection of claims 91 and 98-105 under 35 U.S.C. § 103(a).

8) Mathies in view of Alajoki, and Werner, and Regnier

Claims 92 and 95 stand rejected under 35 U.S.C. § 103 as allegedly being unpatentable over the Mathies application in view of the Alajoki and Werner applications as applied to claims 90 and 93, and further in view of U.S. Pat. No. 6,156,273 ("the Regnier patent"). The Office Action asserts that the combination of Mathies, Alajoki and Werner discloses all of the required elements of Applicants' claimed invention as applied to claims 90 and 93 except for the inclusion of the use of a micromanifold. The Office Action then looks to the Regnier patent to supply a micromanifold to form Applicants' claimed invention. Applicants respectfully traverse the rejection because there is no motivation to combine the references in the manner urged by the Examiner and because the combination of references does not disclose, teach or suggest the Applicants' claimed invention.

As Applicants described with respect to the nonobviousness discussion above, all of the claims dependent on claim 1, such as claims 90 and 93, are non-obvious with respect to the combination of the Mathies and Alajoki applications. Moreover, the additional combination of the Werner application does not render claims 90 and 93 obvious for the reasons given above. Accordingly, the additional combination of the Regnier patent's disclosure pertaining to micromanifolds still does not overcome the deficiencies of the combination of the Mathies, Alajoki and Werner applications, namely to provide a microarray and an observation port through which at least one target disposed within the microarray is capable of being detected. Thus, the combination of the disclosures of Mathies, Alajoki, Werner and Regnier would not produce any claimed invention.

Because the combination of references does not disclose, teach or suggest all of the required elements of the claimed invention, Applicants submit that Mathies in view of Alajoki, further in view of Werner, and further in view of Regnier does not render obvious the claimed invention and requests withdrawal of the rejection of claims 92 and 95 under 35 U.S.C. § 103(a).

III. Conclusions

Applicants request the Examiner to:

- (1) enter the amendments to the specification at paragraph [0060];
- (2) reconsider and withdraw the rejections of the claims; and
- (3) pass claims 1-114 to allowance.

DOCKET NO.: SNL-0004 (SD-8433)
Application No.: 10/701,097
Office Action Dated: January 25, 2006

PATENT

If the Examiner wishes to discuss this matter further, she is requested to contact the undersigned attorney at 215-568-3100.

Respectfully submitted,



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Date: June 26, 2006

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